

REMARKS

Claim Amendments

Claims 1, 3 - 8, and 10 - 13 have been canceled. Claims 14-27 are withdrawn.

Claim 2 has been amended to include the limitations of Claims 3-8 and to clarify the molecular weight of the poly(caprolactone). The self-crosslinkable feature of the present invention provides for crosslinking in the absence of a crosslinking agent. This aspect is disclosed in the present specification in numerous places, for example: the Title, the Abstract, in the Specification on pages 2-3, paragraphs [0013], [0014], [0017], [0025] [0027]-[0030], etc. The other limitations are also supported in the specification. Claim 9 depends directly from Claim 2. The following remarks in response to the art rejections are respectfully provided to clarify the subject matter claimed by the present invention and to patentably distinguish the claims from the cited references.

Art Rejections

Claim 2 was rejected under 35 USC 102(b) as being anticipated by Wiggins, "Design of bioabsorbable, amorphous polymer networks and composites" ("Wiggins"). Wiggins has prepared poly(D, L-lactide-co-[epsilon]-caprolactone) fumarate. The transitional phrase "consisting essentially of" in amended claim 2 excludes lactide groups as in Wiggins.

In meeting Applicants' burden to establish that a specified material practiced in a prior art reference is excluded for Applicants' claims by the "consisting essentially of" claim language, Applicants' submit the following

discussion of inventive features of the present invention and that the specific materials cited in the prior art references are excluded by the claim language. One basic and novel characteristic of the present invention, for example, amended Claim 2 is a flexible, injectable, self-crosslinkable copolymer consisting essentially of: caprolactone units; and fumarate units, wherein the copolymer is prepared by reacting (i) poly(caprolactone) and (ii) fumaric acid or a salt thereof, and wherein the poly(caprolactone) has a number average molecular weight in the range of 500-10000 daltons, and wherein the copolymer has a number average molecular weight in the range of 3000 to 4000, and a polydispersity index in the range of 2 to 4, a melting point in the range of 50°C to 70°C, and a hardening point in the range of 30°C to 40°C, and wherein the copolymer is injectable at temperatures above the melting point. Claim 2 clearly does not claim the lactide groups of Wiggins.

One basic inventive aspect of the present invention as claimed is that it is flexible and injectable, see disclosure paragraphs [0024] - [0026] and [0051], for example. This point is critical in that the “consisting essentially of” claim language of Claim 2 specifically excludes the lactide groups of Wiggins to avoid the adverse results that Wiggins materials possess in contrast to the present invention. For example, the lactide groups of Wiggins may adversely affect the softening temperature of a polymer. See page 3, lines 23-25 of the present specification.

In fact, Wiggins itself teaches in the Abstract that “[n]etworks synthesized from D, L-lactide based precursors were more rigid with higher tensile strengths

and moduli, while networks synthesized from [epsilon]-caprolactone were more flexible and elastomeric.” [underlining added] Thus, the lactides in Wiggins that produce rigid networks actually teach away from the material claimed in the present invention which provides the inventive benefits of flexibility and injectability.

Also, Wiggins does not teach a self-crosslinkable copolymer as claimed in Claim 2 of the present invention. It is submitted that the rejection under Wiggins has been overcome by the above discussion and the amendments to Claim 2.

Claims 2 and 9 were rejected under 35 USC 102(b) as being anticipated by Chung *et al.*, European Polymer Journal, 39, 1817-1822 ("Chung"). Chung has prepared polycaprolactone trimethacrylate di(propylene fumarate)-dimethacrylate (PCL900TMA/DPFDMA). The two materials disclosed in Chung, namely: 1) di(propylene fumarate)-dimethacrylate (DPFDMA); and 2) polycaprolactone trimethacrylate (PCLTMA), both include methacrylates. The transitional phrase "consisting essentially of" in amended claim 2 excludes methacrylate groups taught in Chung. Claim 2 simply does not claim the methacrylate groups of Chung.

Another basic inventive aspect of the present invention as claimed is that it is biodegradable, bioresorbable and biocompatible, see disclosure paragraphs [0025] - [0028], for example. This point is critical in that the "consisting essentially of" claim language of amended Claim 2 specifically excludes the methacrylate groups of Chung that may adversely affect the biodegradability of a polymer.

The degradation behavior of the present invention as described in paragraph [0015] of the specification is another basic inventive aspect of the present invention. The methacrylics present in Chung's and Fisk's polymers that possibly form polymethacrylates have poor biodegradability in direct contrast to the excellent biodegradability, bioresorbability and biocompatibility of the present invention as claimed in Claim 2. Again, the "consisting essentially of" claim language in Claim 2 specifically excludes the methacrylates of Chung and Fisk to provide the claimed benefit of excellent biocompatibility of the present invention.

Also, Chung does not teach a self-crosslinkable copolymer as claimed in Claim 2 of the present invention. The interpenetrating network in Chung was achieved by reacting two materials DPFDMA and PCLTMA.

It is submitted that the rejection under Chung has been overcome by the amendments to Claim 2. Claim 9 is also submitted to be patentable over Chung in view of the amendments to Claim 2 from which it depends.

Claim 2 was rejected under 35 USC 102(b) as being anticipated by U.S. Patent No. 4,082,816 to Fisk *et al.* ("Fisk"). Fisk has prepared a coating composition by "polymerizing a mixture of vinyl monomers, including at least one monomer containing a -COOH and/or -OH functional group, with ϵ -caprolactone" (column 1, lines 65-68 of Fisk, underlining added). Throughout the Examples of Fisk either an acrylate or a methacrylate monomer is used. In contrast to Fisk, the present invention does not use an acrylate or a methacrylate monomer, but instead starts with a caprolactone macromer or oligomer of low molecular weights.

Again, the transitional phrase "consisting essentially of" in amended claim 2 excludes the mixtures of vinyl monomers as in Fisk. The vinyl monomers of Fisk are plainly excluded by amended Claim 2. As discussed above with respect to Chung, the acrylate or methacrylate groups of Fisk may adversely affect the biodegradability of the polymer.

The acrylate or methacrylates present in Fisk's polymers that possibly form polymethacrylates have poor biodegradability in direct contrast to the excellent biodegradability, bioresorbability and biocompatibility of the present invention as claimed in Claim 2. Again, the "consisting essentially of" claim language in Claim 2 specifically excludes the methacrylates of Fisk to provide the claimed benefit of excellent biocompatibility of the present invention.

Also, Fisk does not teach a self-crosslinkable copolymer as claimed in Claim 2 of the present invention. It is submitted that the rejection under Fisk has been overcome by the amendments to Claim 2.

Claims 2-7 were rejected under 35 USC 102(b) as being anticipated by U.S. Patent No. 5,747,605 to Breant *et al.* ("Breant"). Breant has prepared polymers in which the "polycaprolactones employed are of high molecular weights and of two types: Tone 767E supplied by Union Carbide Company, of melt index of 30 dg/min, measured at 190.degree. C. under a 2.16-kg load. Capa 680, supplied by Solvay Interlox, of molecular mass of 80,000...." (See column 6, lines 55-62 of Breant. Underlining added.) The Tone 767E polycaprolactone has a molecular mass of 76,000 [see U. S. Patent 7,189,413 B2 to Calias *et al.*

issued March 13, 2007 ("Calias"]]. (This reference is being submitted in a concurrently filed Information Disclosure Statement by Applicants.)

Calias states in column 3 lines, lines 50-58:

"A variety of molecular weights in polycaprolactones is commercially available from Union Carbide Corporation under the Tone brand name. For example, lower molecular weight polycaprolactones are available as Tone Polyols, while higher molecular weight polycaprolactones are available as Tone PCL-300, Tone PCL-700 and PCL767E which have weight average molecular weights of 15,000, 40,000 and 76,000 respectively, as reported by the manufacturer."

Thus, the Union Carbide Tone 767E polycaprolactone used in Breant has a weight average molecular weight of 76,000.

Claim 2 requires using a poly(caprolactone) having a molecular weight in the range of 500-10000 daltons. The molecular mass of 80,000 of the Capa 680 is clearly greater than the claimed range in Claim 2, and the 76,000 of the Tone 767E is also far outside the claimed range of the present invention. The molecular weight recited in Claim 2 is well below the polymers used in Breant.

Further, the Examiner's rejection of Claim 2 in view of Breant based upon the assertion that Breant's polymer must inherently have similar molecular weight characteristics to the present invention is not supported by the disclosure in Breant. The Examiner's assertion is also refuted by the specific material data presented in Calias that the Tone 767E polycaprolactone has a published weight

average molecular weight of 76,000 according to the manufacturer Union Carbide. Clearly in fact, Breant directly contradicts the specific limits on the molecular weight range of 500-10000 daltons in Claim 2 where Breant specifically states that the polycaprolactones employed are of high molecular weights. Also, the material specifications given above are specific proof of this fact.

In addition, the high molecular weight polymers used in Breant may increase viscosity and softening temperature above that suitable for tissue engineering applications. A further inventive aspect of the present invention is that it is flexible and injectable as claimed in amended Claim 2. The lower the molecular weights, the more flexible and less viscous the resulting material. This also enhances the inventive benefit of the present invention of ease of injectability of the claimed material. In complete contrast to the benefits of the present invention, the high molecular weights of Breant would produce more rigid and viscous and less flexible materials.

Also, Breant does not teach a self-crosslinkable copolymer as claimed in Claim 2 of the present invention. It is submitted that the rejection under Breant has been overcome by the amendments to Claim 2.

Claim 9 was rejected under 35 USC 103(a) as being unpatentable over Breant. Applicants maintain that the underlying product of Claim 2 is patentable for the above reasons, so claim 9 which depends from Claim 2 is also patentable.

Claim 9 was also rejected under 35 USC 103(a) as being unpatentable over Kweon, Biomaterials, 24 (2003) 801-808 ("Kweon") in combination with

Chung. As detailed above, Chung fails to disclose a copolymer consisting essentially of caprolactone units and fumarate units as recited in amended Claim 2. Kweon describes a polymer formed by reacting acryloyl chloride and polycaprolactone. In contrast, the present invention uses fumaryl chloride which contains unsaturated carbon-carbon double bonds that can be used for in situ cross-linking. The fumaryl chloride is copolymerized with biodegradable poly(caprolactone) macromer that has a flexible backbone such that the resulting copolymer may self-crosslink in the absence of a crosslinking agent.

Given the formula of acryloyl chloride in Kweon, it is believed that the reaction of Kweon will produce a copolymer with acrylate groups, not fumarate groups as in the present invention. Additionally, the biodegradability problems with acrylate groups were discussed above.

Also, neither Kweon nor Chung teaches a self-crosslinkable copolymer as claimed in Claim 2 of the present invention. It is submitted that Kweon fails to make up for the deficiencies of Chung and therefore, the rejection under Chung and Kweon has been overcome by the amendments to Claim 2. Applicants maintain that the underlying product of Claim 2 is patentable for the above reasons, so Claim 9 which depends from Claim 2 is also patentable.

Chung Not Prior Art

In addition to the arguments made above, Applicants further respectfully submit that Chung is not prior art to the present invention. Chung was published in the European Polymer Journal, Volume 39, Issue 9 in September 2003. Applicants' maintain that their invention disclosure MMV-03-044 was completed

and submitted no later than April 10, 2003 and possibly earlier. Applicants are prepared to provide proof in a Declaration under 37 CFR 1.131 to “swear behind” the Chung reference. For these reasons, Applicants respectfully submit that Chung does is not prior art and does not anticipate the claims of the present invention on its own or in combination with any other reference(s).

Conclusion


This filing of the submission for the Request for Continued Examination requires a fee of \$405.00 set forth in §1.17(e), which is being submitted prior to the payment of the issue fee. A fee of \$555.00 for a three-month extension of time (37 CFR 1.17(a)(3)) is believed to be needed for this amendment. A check for \$1,140.00 is enclosed along with a PTO/SB/22 Petition for Extension of Time under 37 CFR 1.136(a). The check also includes the fee of \$180.00 set forth in §1.17(p) for submission of the Information Disclosure Statement filed herewith. The fees are for those of a small entity. Such status is submitted to be proper as explained below.

Small Entity Status

This is an assertion of entitlement to Small Entity Status under 37 CFR 1.27. Assignee of this application which issued as United States Patent No. 6,884,432 on April 26, 2005 is Mayo Foundation for Medical Education and Research (“MFMER”). FMER is a 501(c)(3) tax-exempt, nonprofit organization that qualifies for Small Entity status under 37 CFR 1.27(a)(3). This patent is also licensed to BonWrx Inc. which also qualifies for Small Entity status under the definition found in 13 CFR 121.801-805, specifically, as a small business concern

with less than 500 employees as defined in 13 CFR 121.802(a). Therefore, the requirements for Small Entity status are met and such status is proper in this application.

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